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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,293	01/09/2001	Thomas E. Wagner	035879-0116	5976

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EXAMINER

LI, QIAN JANICE

ART UNIT PAPER NUMBER

1632

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/756,293

Applicant(s)

WAGNER ET AL.

Examiner

Q. Janice Li

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32,35,36,41 and 44 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32,35,36,41 and 44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 January 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

The amendment and response filed 10/3/03 have been entered. Claims 33, 34, 37-40, 42, 43 have been canceled. Claims 32, 35, 36, 41 have been amended. Claims 32, 35, 36, 41, and 44 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 10/3/03 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32, 35, 36, 41, and 44 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record and following.

With respect to the rejection of claim recitation "the *diversity* of the starting cell populations is preserved in the resultant hybrid cell population", applicants argue that the diversity means tumor diversity/heterogeneity, which is well known in the art.

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Applicants submitted three references (Exhibit 1-3) and a Declaration of Dr. Wagner to support the argument.

The argument and declaration have been fully considered but they are not persuasive. This is because the term *diversity* of the starting cell population encompasses various traits of the tumor cells and antigen-presenting cells. The traits could be the diversities of DNA content, chromosome aberrations, proliferative status, the intratumor heterogeneity, and the invasive growth state of tumor cells such as those taught by the exhibits 1-3. In light of the specification, the utility of making the hybrid cells is enhancing tumor antigen presentation for vaccination, the characteristics such as proliferative states and invasiveness of the tumors are not desired, only the diversity of surface antigens useful for eliciting an immune response against tumors is desired for preservation. In the Declaration, the experimental data confirm the preservation of tumor antigen diversity, but not other diversity. Therefore, if the term means surface antigen diversity, the claim should make this clear. Since, in patentability context, claims are to be given their broadest reasonable interpretations, and since limitations are not to be read into claims from specification. In re Van Guens, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claims must, under modern claim practice, stand alone to define invention.

Accordingly, the rejection stands.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 32, 35, 36, 41, and 44 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In point A of the response under this provision, applicants indicated that they have amended claims 32 and 44 to address the issues raised in the last Office action. However, it is noted that claim 44 has not been amended as indicated, thus, the rejection stands.

In point B of the response under this provision, with respect to the claim recitation "the *diversity* of the starting cell populations is preserved in the resultant hybrid cell population", applicants presented the same argument as in the section of § 112, 1st paragraph, which has been addressed above. Accordingly for reasons of record and those set forth in the immediate preceding section, since the claims have not been made clear what type of diversity they refer to, the rejection stands.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32, 35, 36, 41, and 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Gong et al* (Nature 1997;3:558-561, IDS), in view *Koolwijk et al* (Hybridoma 1988;7:217-225).

In 10/3/03 response, applicants argue that *Gong et al* and *Koolwijk et al* fail to teach or suggest every limitation of the present invention, particularly they fail to teach the diversity of the starting cell population is preserved. Applicants argue that *Gong et al* teach using his method for un-characterized tumor antigen, and is not a reference for preservation of population heterogeneity.

In response, it is noted that the teaching of using hybrid cells for un-characterized tumor antigens is a teaching of the diversity of the starting cell population, that the skilled in the art knows to use the diverse uncharacterized antigens of the starting tumor cell population for tumor vaccination, and the fact that *Gong et al* succeeded in inducing anti-tumor activity with the hybrid cells indicated that the antigenic diversity of the starting tumor cell population has been at least partially preserved in the hybrid cells. It is also noted that *Gong et al* reference is relied upon as a showing that fusing tumor cells and dendritic cells to make a vaccine composition for anti-tumor effect, after all, the claimed method is for preparing a cancer vaccine, not preserving the diversity of the starting cell population. Therefore, even though applicants submitted a Declaration of Dr. Wagner presenting experimental data showing that by HAT selection of a fusion between dendritic cells and tumor cells, certain antigen or marker was lost over 20 days

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culture period, the combined teachings of *Koolwijk et al* and *Gong et al* still teach the claimed method steps, which would intrinsically preserve the diversity of the starting cell population, and meet claim limitation. Further, because there is no limitation on what kind of diversity and the degree of diversity that is required, *Gong et al* reference still meet claim limitation. On a different aspect, it is noted that the experimental data of the Declaration was done for hybrid cells between dendritic cells and tumor cells, whereas claim 32 recites antigen-presenting cells, which encompass broader cell types. The specification or Declaration fails to teach whether this would be true for most types of antigen-presenting cells beyond dendritic cells.

Second, applicants argue that there is no reasonable expectation of success in combining the teachings of *Gong et al* and *Koolwijk et al* to arrive at the present invention. A person of ordinary skill in the art would know that the method of *Gong et al* does not maintain the diversity of the starting cell sub-populations, that the Examiner is at best using an improper "obvious to try" standard. In response, it is noted the Office uses a different reasoning for combining the references, thus not a standard of "obvious to try". In Examiner's opinion, the evidence regarding HAT selection method would not fully preserve the surface antigen of the starting cell population is provided by the applicants' Declaration, there is no evidence that a person of ordinary skill in the art would know that the method of *Gong et al* does not maintain the diversity of the starting cell sub-populations. In fact, if *Gong et al* know such fact, it would have been another motivation of using the two-dye cell sorting system for selecting hybrid cells. Here, the

motivation to combine references is not relied on preserving diversity but the efficiency of the process. This leads to the next argument.

Finally, applicants argue that there is no suggestion either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art to combine the teachings. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 19880; *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). The Office has repeatedly cited the teaching of *Koolwijk et al* for the motivation of using a different method for hybrid cell-selection, i.e. "THE MAJOR ADVANTAGE OF THIS METHOD OF *HYBRID* HYBRIDOMA ISOLATION OVER THE METHOD USING MUTANT PHENOTYPES AND A BIOCHEMICAL SELECTION AFTER FUSION IS THE FAST ISOLATION PROCEDURE. NO TIME-CONSUMING ISOLATION OF THE MUTANT PHENOTYPES BEFORE FUSION IS NEEDED. *AFTER FUSION, THE BIOCHEMICAL SELECTION PROCEDURE IS NOT NECESSARY*" (see Introduction and Discussion, emphasis added). Thus, *Koolwijk et al* provided motivation for selecting hybrid cells using a two-dye cell sorting system. In 10/3/03 response, applicants argue that cutting steps and saving time is by no means the driving force, instead, a person of ordinary skill in the art would chose the method that achieved the most accurate results. In response, saving time and cost has always been the motivation for improvement in the advance of all fields of technology. Since there is no teaching or suggestion in *Koolwijk et al* or *Gong et al* that the two-dye

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cell sorting system would be less accurate in hybrid cell selection compared to the biochemical selection, there is nothing preventing the skilled artisan to use a method less costly, and more efficient. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the methods taught by *Koolwijk et al*, in the process for selection and purification of dendritic-tumor cell hybrids of *Gong et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the method because the double fluorescent cell sorting requires fewer steps and less time for making and selecting hybrid cells. The hybrid cells selected by the method would intrinsically have the diversities of the starting cell population. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

For reasons of record and those set forth foregoing, the rejection stands.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is **703-308-0196**.

Q. Janice Li
Patent Examiner
Art Unit 1632


January 26, 2004

